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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,611	02/08/2002	Brian Leyland-Jones	3298.1001-000	1456

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,611	LEYLAND-JONES, BRIAN	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/8/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *31-50,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30,51 and 54-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 4/8/2004 has been received and entered into record and considered. The following information provided in the amendment affects the instant application:

1. Claims 32-34, 37-39, 41, 43, 52 and 53-54 have been amended.
2. Claim 57 has been added to the instant application.

Election/Restriction

The newly added claim 57 directs to an assay system is accordingly grouped to invention VI. Applicant's election with traverse of Group I on 4/8/2004 is acknowledged. The traversal is on the ground(s) that inventions of Groups I-VI are dependent and related to each other and, therefore, should be rejoined (pages 3-5 of the Response). These arguments have been found to be not persuasive because an application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP §806.04 - 806.04(i)) or distinct (MPEP §806.05 - 806.05 (i)). The Examiner has shown that the Groups I -VI are independent or distinct for the reasons in the previous Office action. Furthermore, MPEP §803 provides that the separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a prima facie case that the search and examination of the plural inventions would impose a serious burden upon the Examiner; such separate classification was set forth in the previous Office action.

The requirement is still deemed proper and is therefore made ***FINAL***.

Claims 31-50, 52-53, and 57 are withdrawn from further consideration pursuant to 37 CFR 1.1421), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 1-30, 51, 54-56 are under examination in the instant office action.

Claim Rejections - 35 USC § 112

Scope of enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-30, 51, 54-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a biological samples, such as saliva, tissue, plasma, urine, serum, blood, nasal mucosa, does not reasonably provide enablement for *breadth* sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant invention asserts a method of characterizing a multi-determinant metabolic phenotype. However, the instant invention fails to provide enough guidance for one skilled in the art on how to practice the instant methods, thereby requiring undue experimentation to discover how to use applicant's invention, as currently claimed.

Applicant is advised that the" biological sample", according to the definition presented on page 62, lines 20-25 of the instant specification, includes "breath" samples. However, there appears to be no disclosure presented in the instant specification, which would provide support for detecting metabolites in breath samples. Applicant disclose a list of assay and sensors, including conductive immunosensor, optical sensor, total internal reflection spectroscopy, ellipsometry, optical waveguide, surface plasmon resonance, TSM, SAW sensor but none of the sensor is known to detect a *volatile breadth* sample. (See page 125-132) It would require undue experimentation for one skilled in the art to discover how to characterize a multi-determinant metabolic phenotype using a breath sample for analysis.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-30, 51, 54-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, line 3, "With respect to metabolic characteristics" is vague and indefinite. It is unclear what is the "metabolic characteristics" in the context.

With respect to claim 3, line 2, "under the curve" lacks antecedent basis.

With respect to claim 3, ratio of area under the curve" is vague and indefinite. It is unclear what is the area under the curve.

With respect to claim 3, "signal peak height ratio" is vague and indefinite. It is unclear what is the "signal peak height ratio" in the context.

With respect to claim 10, "molecular imprinted polymer" is vague and indefinite. It is not clear what is the molecular imprinted polymer.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-6, 26-30, 51, 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Desta et al. (Clinical Pharmacology and Therapeutics 1999 65: 10-20).

Desta et al. teach a method of evaluating the effect of antibiotics clarithromycin on the metabolism of pimozide on individuals suffered with Gilles de la Tourette's. (See abstract) Desta et al. use pharmacokinetic analysis, including concentration-time curve, terminal half-life, clearance and volume distribution, peak and ratio, to measure the metabolites in the plasma from the individuals dosed with the pimozide, antibiotics or both. (See Methods; Data analysis; Figures 1-3) The metabolic enzymes involving in the metabolisms are CYP2D6 and CYP3A. (See abstract; Introduction) The magnitudes and variations of metabolites reflect the multi-determinant metabolic phenotype with respect to the therapeutic agents. (See Table I- III) The goal of the study is to have clinical application, e.g. with considerations of the metabolic profile of the therapeutics, to optimize the chemical treatments on the Tourette's patients. (page 19, second paragraph) It is also inherently precautious measures in clinical practice, including drug resistance, susceptibility, and renal function when patients are to be treated with antibiotics.

7. Claims 1-10, 14-15, 18, 25-30, 51, 54-56 are rejected under 35 U.S.C. 102(a) as being anticipated over Wainer et al. (J Pharm. Biomed. Anal. 1995 13: 1079)

Wainer et al. teach using probe drugs, such as caffeine to study phenotypic characteristics of NAT2 (N-acetyltransferase-2) in individuals. (See abstract) Wainer et al. teach that administering the probe drugs to individual and analyze the plurality of metabolites from urine samples, i.e. AAMU to 1-methylzanthine (1X), corresponding to the metabolic profile of the individuals in response to the probe drug. (See Table 2) Wainer et al teach a rapid and convenient ELISA assay instead of conventional HPLC. (See Method and Materials) The assay involves using polyclonal antibodies against the phenotyptic determinants in response to the probe drugs. (See Materials and Method)

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wainer et al. in view of Cubicciotti et al. (US 6287765).

Wainer et al. reference has been discussed but does not explicitly teach using aptamer or receptor for drug metabolites study. Cubicciotti et al. reveal that it is known in the art that aptamer or receptor would bind to the therapeutic metabolic target, and therefore can be detected by modified ELISA increase sensitivity, cost-effectiveness and reproducibility. (See example 21 and example 22) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Wainer et al. with the affinity complexation agent as taught by Cubicciotti et al. since it is

known in the pharmaceutical practice to detect the binding of receptor or aptamer to the target compound to increase sensitivity, cost-effectiveness and reproducibility.

11. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wainer in view of Beste et al. (PNAS 1999 96: 1898-1903)

Wainer reference has been discussed but does not explicitly teach using anticalin for binding assay. Beste et al. teach that using lipocalin as an alternative for conventional antibodies for ligand binding assay. (See abstract) Beste et al. reveal that conventional antibodies have certain disadvantages such as larger molecules not easy to manipulate, or two polypeptide chains complicate cloning procedure. (page 1898, left column, first paragraph) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Desta and Wainer et al. with the alternative anticalin as taught by Beste et al. for convenience and economy in detecting the target molecules.

12. Claim 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wainer in view of Pronovost et al. (US 5786220).

Desta and Wainer references have been discussed but do not explicitly teach using dipstick immunoassay to detect metabolites in a sample. Pronovost et al. teach using dispstick for quick detecting the presence of metabolites in patient sample. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Desta and Wainer et al. with dipstick immunoassay as taught by Pronovost et al. to detect metabolites in a patient sample in a time-saving manner.

13. Claims 18-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wainer et al., in view of Rabbany et al. (Critical Reviews in Biomedical Engineering 1994 22: 307-346).

Wainer et al. reference has been discussed but does not explicitly teach using various biosensors for detection purposes. Rabbany et al. review the immunosensors in applications to the detection of analytes in samples, including optical, piezoelectric, electrochemical sensors. (See page 320-340) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Wainer et al. with alternative biosensors as taught by Rhbbany et al. since it is known in the art to use the biosensor to detect target molecules in the sample.

14. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wainer, in view of Wang et al. (Anal. Chem. 1997 69: 5200-5202).

Wainer et al. reference havs discussed but does not explicitly teach using quartz crystal microbalance (QCM) to detect peptide nucleic acids. Wang et al. teach using QCM biosensor to detect DNA-protein complex in a biological sample. (See abstract, page 5200, right column, second paragraph) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Wainer et al. with the aid of QCM biosensor as taught by Wang et al. for the detection of aptamer complex, e.g. DNA-protein-metabolites, in the patient plasma sample to determine the phenotype of the patient in response to the treatment of therapeutics.

Conclusion

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-282-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

June 3, 2004

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06/14/04